OTGM 3 Outline

Ch 159B – Symptom assessment and management at the end of life

Authors:
Nele Van Den Noortgate
Elizabeth Sampson

Ch 159B-01: Epidemiology of symptoms in the older population with advanced chronic disease

The ageing population is associated with growing numbers of people suffering from a complex combination of chronic diseases such as heart disease, cerebrovascular disease, respiratory disease, cancer, frailty and neurodegenerative diseases such as dementia. This increasing complexity and changing pattern of illness gives rise to some particular needs at the end of life. In a study performed in community-dwelling older persons with advanced chronic disease Walke et al. (2004) reported that virtually all participants (86%) experienced at least one symptom and most (69%) experienced two or more symptoms. The symptoms reported commonly in studies are limited activity (61%), fatigue (47%) and physical discomfort (38%) like pain, urinary incontinence, anorexia, constipation and dyspnoea (Van Lancker *et al*. 2014). Also in people with advanced dementia, multiple clinical care needs like eating and swallowing disorders (from 45.9% to 85.8%), pressure ulcers (in 14.7% to 62.3%), urinary incontinence (in 89.2%), and different types of infection (13.4% to 52.6%) are described. Most reported physical symptoms at the end of life in population with advanced dementia are pain in 11.5% to 64.7% , shortness of breath in 8.2% to 46% and agitation in about 55% of the population with advanced dementia (Mitchell *et al*. 2004,2009; van der Steen *et al*. 2009; Hendriks *et al*. 2014; Vandervoort *et al*. 2013; Sternberg *et al*. 2014).

Symptoms during the last year of life in older persons are often more complicated than in younger patients. Older persons not only suffer from symptoms due to the underling life-threatening illness but also from consequences of other chronic conditions like osteoarthritis,

osteoporosis, and peripheral neuropathy. Moreover psychosocial and spiritual needs, related to other life events such as bereavement and not directly to the underlying life-threatening disease, can cause other forms of suffering. Between 27% - 66% of patients with advanced dementia experience psychological symptoms such as behavioural disturbances and psychosis. Also anxiety and depressed mood occur in 30% to 50% of the older population with cancer as well as with advanced dementia (Van Lancker *et al.* 2014, Hendriks *et al.* 2014). Spiritual symptoms as a cause of suffering are rarely studied. One recent study in patients with advanced dementia found only 56% of the residents die peacefully as perceived by relatives (De Roo *et al.* 2014).

Geriatric palliative medicine is the medical care and management of older patients with health related problems and progressive, advanced disease, for whom the prognosis is limited and the focus of care is the quality of life. Therefore geriatric palliative medicine should focus on geriatric assessment, relief from pain and other symptoms and management of physical and psychological problems, integrating social, spiritual and environmental aspects. It should also recognise the unique features of symptom and disease presentation, the interaction between diseases, the need for safe drug prescribing and the importance of a tailored multidisciplinary approach for older palliative patients and their family (Pautex *et al.* 2010).

A recent white paper from the European Association of Palliative Care (EAPC) reviews the aspects of palliative care for patients with dementia and formulates some recommendations for clinical practice and future research (van der Steen *et al.* 2014).

In this chapter we will focus on the assessment and the management of common symptoms such as pain, anorexia, nausea and vomiting, constipation, delirium, depression and anxiety in older persons with normal and impaired cognitive function.

Ch 159B-02: A palliative approach in older people

Palliative care has been defined by the World Health Organisation as:

"The active, total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social and spiritual problems is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families."

This definition provides a useful framework for thinking about management in older people who are reaching the end of life. It should be emphasised that palliative care does not mean withdrawing care or not using "curative" therapies, for example, whilst an older person and their family may not have opted for "aggressive" interventions it may be reasonable to alleviate a bowel obstruction or have other surgery, if the problem is causing distress or pain.

It is vital that a holistic and multidisciplinary approach is taken towards the end of life. The older person may benefit greatly from environmental modifications in the home such as bath boards or stair lifts and these interventions can decrease pain, improve independence, function and subsequently quality of life. As death approaches the incidence of swallowing difficulties, cachexia and pressure sores may increase (Ahronheim *et al*. 1996) and the expertise of other members of the multidisciplinary team such as tissue viability nurses, speech and language therapists and dieticians is important.

A palliative care approach ensures that symptoms are continually assessed and it is important that goals of treatment are regularly reviewed and recalibrated as the end of life approaches. This may mean, for example that the use of opioid and sedation becomes more acceptable to the dying older person if it means that pain is well managed, and conversely they may accept a degree of pain if this allows them to continue to communicate (Russell *et al.* 2010).

It can be helpful to have discussions with the dying person and their families about a "ceiling of care" to develop a treatment escalation plan (Obolensky *et al.* 2010). This promotes good pain management by considering decisions, for example, discontinuing painful interventions like phlebotomy or arterial blood gas sampling. It may also reduce the risks of people undergoing painful and distressing transfers towards the end of life, particularly into acute care settings.

Towards the end of life, the role of families and other informal caregivers becomes more vital. As well as providing physical care and support they may need to act as an advocate or key decision maker, especially if the dying older person loses the capacity to communicate. They may have to give information on medical comorbidities, ensure that analgesia are given regularly and help interpret and communicate when the person is in pain.

Ch 159B-03 Assessment of symptoms and discomfort at the end of life

As diseases become more and more complex and present with atypical symptoms, it is important to perform a thorough assessment of possible symptoms. Scales such as the Edmonton Symptom Assessment Scale and adapted versions can be helpful in examining the presence and the intensity of common symptoms in advanced disease (Walke *et al.* 2006). For pain assessment in the older people, please refer to chapter 159A-03. This assessment should be followed by extended history taking, an in depth clinical examination and where necessary, appropriate investigations such as a biochemical profile, full blood count or a radiology.

Distinguishing between pain and discomfort is important in providing the best quality care to older people. Significant pain will usually result in discomfort, but it is important to understand that pain is just one of many possible causes of discomfort; for example being bored, agitated, cold or constipated. In addition, comfort is more than the absence of discomfort (mental or physical), or pain and is also closely related to the concept of quality of life.

A number of discomfort scales have been developed for example, the Discomfort Scale–Dementia Alzheimer Type "DS-DAT" (Hurley *et al.* 1992) and the End of Life in Dementia-Comfort Assessment in Dying scale "EOLD-CAD" a tool developed to assess comfort in dementia at the end of life (Volicer *et al*. 2001). These tools include broader concepts than pain tools (although many include items related to physical pain as well) and include constructs such as "peace", "serenity" (EOLD-CAD) and "frightened facial expression: scared, concerned looking face; looking bothered fearful or troubled; alarmed appearance with open eyes and pleading face (DS-DAT).

A different approach is taken in some tools, for example the Disability Distress Assessment Tool (DisDAT) was developed for people with severe communication difficulties and documents an individuals' signs and behaviors when distressed and when they are content or neutral. This allows a more person-centered assessment of distress and discomfort but requires raters to have individual knowledge of a person's individual response (Jordan *et al.* 2012).

Ch 159-4 Management of pain and prevalent non-pain related symptoms in advanced disease

Palliative radiotherapy and chemotherapy may be an option for older patients in order to achieve better symptom control but in this population careful consideration of benefits, risks and a careful observation for adverse events is vital. Currently, there is only limited research concerning palliative radiotherapy and chemotherapy in the older person.

Good pain and symptom control must be based on the four following key domains: physical, psychological, social and spiritual wellbeing. If one domain is forgotten, controlling pain and other symptoms becomes even more challenging.

When considering symptom control at the end of life, it is important to understand that listening and being present may be more important than just prescribing medication. Explaining the

reasons for symptoms and the planned actions to alleviate or resolve them is often enough to reassure patient and family members. Non-drug methods, as discussed below, may have an important place in the treatment of the older palliative patient. In case of pharmacological therapy, a careful follow-up of the possible adverse side effect is essential.

In the next part of this chapter, we will briefly consider the management of common symptoms in the older population.

Pain

For the basic principles of pain treatment in older people, please refer to chapter 159-04.

In palliative medicine, special attention should be paid to the 'total pain' concept, exploring the non-physical components that may influence the perception of pain and suffering. Psychological distress including depression and anxiety is common in older people who may be nearing the end of life. In particular, at the end of life, people may experience existential distress - feelings of hopelessness, meaninglessness, or anxiety over dying. A holistic, multidisciplinary approach, such as that provided by palliative care services, may offer meaningful support.

Anorexia – cachexia syndrome

The anorexia-cachexia syndrome (ACS) is characterised by anorexia, malnutrition, weight loss, asthenia and chronic nausea. It is one of the most frequent symptoms in palliative care and the cause of death in more than 50% of the cases. Moreover anorexia is an independent predictive factors for successful treatment and patient quality of life. ACS is characterised by a complex underlying pathophysiology (Argiles *et al*. 2003). Possible underlying pathogenetic factors in this syndrome include circulating cytokines such as interleukin 1(IL-1), IL-6, tumour necrosis factor-α, interferon α and γ, secreted by the tumour or the host itself. Recent studies show that these factors are also present in patients with terminal heart failure, terminal chronic obstructive lung disease and possibly in patients with dementia.

The treatment of ACS is still a challenge. Dietary advice, enteral and parenteral nutrition have not been shown to influence the wellbeing and survival of the cancer patient. Synthetic progestogens are a class of drugs with possible benefit in the ACS. These molecules induce a significant increase in the appetite and sometimes also increase the weight of the patient. However those drugs have not been shown to improve lean body mass, functional activity or quality of life (Ruiz *et al.* 2013). Moreover they have important side effects such as fluid retention and high risk of phlebothrombosis: these are often a contraindication to their use in older patients. Another effective agent, corticosteroids may be useful for their rapid beneficial effects on appetite, mood and quality of life. However, because of their side effects (muscle atrophy, increased risk of glucose intolerance and candida infection) and rather short term effect, alternating administration is recommended. Among the drugs with confirmed clinical efficacy, COX-2 inhibitors and anabolic agents, such as oxandrolone, have been shown to achieve good results, however no specific studies are available in older people. Investigational drugs with so far proven clinical effectiveness include ghrelin and ghrelin mimetics, SARMs, myostatin inhibitors and β-adrenoceptor agonists (Mantovani *et al*. 2013).

Fatigue

Fatigue is often present in people receiving palliative care. The unusual need for increased rest and sleep, difficulties with concentration, a diminished attention and impaired problem solving ability often influence the quality of life. Fatigue is often accompanied by complaints as hypotension, bradycardia, dyspnoea and dizziness. The aetiology is often multifactorial. Treatment focusses on the management and correction of possible causal factors. Supportive measures such as an activity diary, including rest, adapting the daily routine and limiting the frequency of visits may be necessary to augment the quality of life. Corticosteroids or synthetic progestogens may be considered but with the same cautions as when they are used in cachexia (Sherman *et al*. 2003).

Dyspnoea

Dyspnoea is a subjective feeling of difficulty in breathing and has multiple underlying causes. These are often multifactorial, may not have a specific treatment and thus symptomatic treatment is required to maintain quality of life.

Non-pharmacological support is important as severe dyspnoea is often frightening and the induced anxiety can further exacerbate the symptom. Listening to patients and their families, careful explanation and reassurance can be helpful for the patient. Relaxation, breathing exercises and help with expectoration of secretions offered by a physiotherapist is important. The use of oxygen is often controversial and only necessary if hypoxia can be demonstrated. Three classes of drugs are useful as pharmacological treatment namely opioids, corticosteroids and benzodiazepines. Opioids act by reducing the sensitivity of the respiratory centre and the central perception of dyspnoea. A Cochrane and another recent review shows evidence for the use of oral and parenteral morphine on the intensity of breathlessness but not on exercise capacity (Jennings *et al*. 2003, Johnson *et al* 2014). Corticosteroids are preferentially used for their anti-inflammatory effects. Benzodiazepines (with preference for short acting) are important drugs to control anxiety.

Nausea and vomiting

Table 2 gives pharmacological treatment options for nausea and vomiting from various causes. The first line treatment in opioid-induced vomiting is metoclopramide, often given prophylactically (Neoh *et al*. 2014).

In patients with nausea, oral medication can be tried but often and especially in vomiting patients, alternative routes are needed. The preferred route in this patients is the subcutaneous way using a syringe driver. Specialist detailed information concerning this mode of drug administration in palliative care is available (Dickman and Schneider 2011).

In addition, non-pharmacological treatment is very important in managing nausea and vomiting. Avoidance of irritating smells, creating a quiet environment, offering fresh air, managing anxiety, avoiding movements and regular mouthwashes with clear fluids, are small interventions that can give relief.

Pathophysiological pathway	**Aetiology**	**Pharmacological treatment**
Gastro-intestinal	Cancer of GI tract Gastro paresis Hepatomegaly Constipation/obstruction Radiation therapy	Metoclopramide 10 – 20 mg/8h PO, SC,IV Domperidone 10 – 20 mg/6à8h PO Dexamethasone 5-20mg/24h SC,IV Somatostatin/octreotide 0.3-1.5mg/24h SC Promethazine 25-50mg/12h SC
Stimulation of chemoreceptor trigger zone	Chemotherapy Opioids, antibiotics, NSAID's … Biochemical: hypercalcaemia, uraemia, infectious, tumour toxins	Metoclopramide 10 – 20 mg/8h PO, SC,IV Domperidon 10 – 20 mg/6à8h PO Alizapride 200-300mg/24h SC,IV Chlorpromazine 25-75mg/8u PO Haloperidol 2-10mg/24u PO, SC, IV 5HT3-antagonist SC, IV, PO
Stimulation of the vestibular apparatus	Cerebral tumour, antibiotics, movements	Hyoscine hydrobromide 0.25-1.5mg/24h SC Promethazine 25-50mg/12h SC
Stimulation of the cerebral cortex	Anxiety Raised intracranial pressure by cerebral tumour, metastasis, cerebral oedema	Dexamethasone 5-20mg/24h SC,IV Hyoscine hydrobromide 0.25-1.5mg/24h SC Lorazepam 4 mg/24u PO,SC,IV Alprazolam 0.25-1mg/8u PO

Table 2: Pharmacological treatment of nausea and vomiting by underlying causes

Constipation

Constipation is a common problem in over 50% of people receiving palliative care, increasing to a prevalence of 80-90% in those on opioid therapy. A recent review on the treatment of

constipation in palliative care concluded that there is little evidence for conventional pharmacological treatments for constipation due to insufficient randomized controlled trials. Subcutaneously administered methylnaltrexone was found to be effective and well tolerated with limited side effects (Clemens *et al.* 2013). A European Consensus Group on constipation in palliative care (2008) recommended a combination of a softener and stimulant laxative but the choice should be made on an individual basis.

Delirium

Most people who are dying will experience delirium. Given that the major risk factors for delirium are increasing age, frailty, pre-existing cognitive impairment and infection, it is very common in older people with terminal illness (Inouye *et al.* 2014). Delirium is a frightening experience, both for the person experiencing it and their families; it also leads to significant management challenges for staff. The core symptoms are an abrupt onset with fluctuating course, alterations in the sleep-wake cycle and impaired level of consciousness. Agitated or hyperactive delirium is particularly common in people who are dying and is accompanied by frightening perceptual disturbances of hallucinations. A palliative care approach is compatible with seeking and treating the cause of the delirium, for example giving an antibiotic for a urinary tract infection may provide symptomatic relief. Non-pharmacological interventions can be very effective and safer in older people. There is good evidence that multi-component interventions involving re-orientation, a quiet and well-lit environment, enhancing vision and hearing by ensuring glasses and hearing aids are available and early mobilization reduces the risk and length of delirium (Inouye *et al.* 2014). In cases of great distress it may be necessary to use medication. Conducting clinical trials in delirium is challenging. A recent Cochrane review has found that low dose haloperidol (0.5-1.0mg, every 2-12 hours, carefully titrated to response and to avoid over-sedation) may be effective in reducing the symptoms of delirium. Older people are at higher risk of adverse side effects from neuroleptics, for example over sedation, aspiration

and stroke and neuroleptics should be used for the shortest possible time and at the lowest effective does (Jackson-Siegal *et al.* 2004). There is less evidence for the effectiveness of benzodiazepines in older people with delirium and their use is not recommended (Young *et al.* 2010).

Depression

Depression is caused by the complex interaction of biological factors, for example Parkinson's, stroke and other neurodegenerative diseases, thyroid dysfunction and anaemia, with psychological challenges, such as loss and grief and social factors such as loneliness and loss of independence. As the end of life approaches the risk of developing depression increases further, for example in a large American population cohort of older people, more than 70% of colorectal cancer outpatients were diagnosed with depressive disorder (Zhang and Cooper 2010).

Depressed mood and sadness may be an appropriate response to imminent death. Standard clinical diagnostic criteria for depression such as DSM IV or ICD 10 may not be useful towards the end of life as they rely heavily on the presence of somatic symptom such as loss of appetite or sleep problems. Multidisciplinary assessment, for example input from an old age psychiatrist or psychologist may be very helpful in disentangling these problems.

Management of depression in older people who are dying requires a bio-psychosocial approach. Ensuring that pain and other physical symptoms are treated adequately may improve mood (Husebo *et al*. 2014). Psychological and supportive therapy can be effective, even in people with early cognitive impairment. Psychotherapy is effective for depressive symptoms in advanced cancer although evidence for effectiveness in major depression is lacking (Akechi *et al*. 2008). There is good evidence that antidepressants are effective in patients with advanced cancer (Rayner *et al.* 2011). The evidence for other life limiting illnesses is less strong, however pharmacotherapy remains the mainstay of treatment in major depression. In older people,

selective serotonin re-uptake inhibitors are the antidepressant of choice as they are effective as tricyclic antidepressants but have a safer side effect profile (Rayner *et al.* 2011). Tricyclic antidepressants are potently anticholinergic and can cause tachycardia, constipation, dry mouth and have effects on cognitive function- all of which highly undesirable in the older person.

Anxiety

Anxiety causes a broad range of symptoms both psychological, for example worry, distractibility or rumination, and physical such as restlessness. These can cause a high level of distress for patients and their families and should be seen as more than just inevitable at the end of life. Anxiety can be precipitated or worsened by the underlying physical problem; pain, dyspnoea, delirium and infection are commonly associated. Anxiety can also be caused by existential distress and other issues: anticipatory grief of dying, feelings of lack of control, claustrophobia and concerns about intimacy.

There have been few studies on how to best manage anxiety in older people who are dying. A calm, listening empathic approach is sometimes all that is required. Religion may have an important part in the life of the older person and involving faith leaders in support and addressing unmet spiritual needs can alleviate patients' distress (Stanley *et al.* 2008).

Pharmacological management of anxiety may involve treating the underlying cause, for examples ensuring adequate analgesia for pain or giving oxygen and opioids in dyspnoea. Benzodiazepines can be useful if prescribing is carefully considered. Shorter acting benzodiazepines are safer but older people are particularly at risk of side effects such as falls, over-sedation and confusion. Midazolam infusion is widely used in terminal agitation and anxiety in the terminal phase of life.

Dry mouth

People receiving palliative care will often experience a dry and painful mouth. Frequent causes include the use of drugs with anticholinergic effects, opioids, dehydration, decreased food

intake and an increase in mouth breathing. Health care workers should especially be aware of these problems in the older person who is functionally dependent.

Good oral hygiene should consist of regular cleaning of the teeth or dentures and mouthwashes with chlorhexidine 0.2%. In disabled patients mouth care may be needed every two hours. Contributing medications should be stopped if possible and the patient should be offered regular drinks. Artificial saliva or stimulation of the salivary glands by citrus sweets, acid drops and chewing gum can be effective. Candida stomatitis is a frequent complication in palliative patients. Treatment with nystatin suspension or fluconazole is indicated (Sykes, 2003). Other plaques in the mouth are often challenging. Careful cleaning of the tongue with a scraper or brush, using yogurt or vitamin C tablets before cleaning can be helpful. Hydration of the lips by using Vaseline or hydrating lipstick can also diminish the sense of dry mouth. (http://www.who.int/hiv/pub/imai/genericpalliativecare082004.pdf)

Care in the last days of life (terminal care)

The correct recognition and management of the last days of life is very important for the patient and their family as this will influence the family's bereavement and the way they will cope with the loss of their loved one. The dying phase can often be diagnosed through a gradual increase in weakness and drowsiness, a decline in mental capacity, a refusal of food or fluids, irregular breathing, cold and mottled extremities and often an exacerbation of existing symptoms as pain, anxiety or restlessness (Kehl *et al.* 2013). These symptoms are comparable with those in younger patient populations (Rashidi *et al*. 2011). In this terminal period a review of the medication and non-pharmacological management is necessary. Drugs that are no longer necessary for symptom relief should be withdrawn and the route of administration should be revised if the patient is not able to swallow anymore.

Frequent symptoms in the last hours of life are pain, restlessness, agitation and death rattle. Death rattle is caused by respiratory secretions which cannot be cleared anymore. This noisy

breathing may be more distressing for the family than for the patient. Giving families information about the origin of the death rattle is the first step in managing this difficult symptom. A current review of the literature showed that there is no evidence supporting the use of anticholinergic drug at the end of life (Lokker *et al.* 2014). However, another recent review suggested that this observation could be confuted by the prophylactic use of these drugs (Mercadante 2014). Anticholinergic medication as hyoscine hydrobromide (0.5 mg/4h SC, IM) or glycopyrronium (200 to 400 µg given every 4 to 6h SC,IM) may be considered if the aim is to diminish the production of respiratory secretions. These drugs can be added to the syringe driver. In the last days of life, other subcutaneous drugs frequently used to alleviate symptoms include opioids such as morphine and psychotropic medications such as midazolam and sometimes haloperidol.

Ch 059-4 Conclusion

The increasing complexity and challenging patterns of illnesses gives rise to complex needs at the end of life. Symptoms are often not just physical, but also encompass potentially unpleasant emotional and spiritual distress. Symptom control starts with an optimal assessment of symptoms using adequate tools, adapted to the cognitive and communicative status of the person. Little or no evidence is available for the non-pharmacological and pharmacological treatment of symptoms in the older person. Guidelines developed by expert panels of national societies may be of help in optimising the treatment. The management of symptoms at the end of life in older people requires excellent knowledge of geriatric medicine, palliative care, empathy, good communication skill and great compassion.